CLAIMS

What is claimed is:

- 1. An isolated nucleic acid which encodes a precursor glucagon-like peptide 1 (GLP-1) comprising mammalian GLP-1 linked to a heterologous signal sequence.
- 2. The isolated nucleic acid of Claim 1 wherein the GLP-1 encoded by the nucleic acid has an amino acid sequence of SEQ ID NO: 21.
- 3. The isolated nucleic acid of Claim 1 wherein the GLP-1 is a modified GLP-1.
- 4. The isolated nucleic acid of Claim 3 wherein the modified GLP-1 encoded by the nucleic acid has an amino acid sequence in which alanine at position 8 is replaced with glycine (SEQ ID NO: 21).
- 5. The isolated nucleic acid of Claim 3 wherein the modified GLP-1 encoded by the nucleic acid has an amino acid sequence selected from the group consisting of: GLP-1 (7-34) (SEQ ID NO: 23), GLP-1(7-35) (SEQ ID NO: 24), GLP-1(7-36) (SEQ ID NO: 25), Va1⁸ -GLP-1(7-37) (SEQ ID NO: 26), Gln⁹ -GLP-1(7-37) (SEQ ID NO: 27), Thr¹⁶ -Lys¹⁸ -GLP-1(7-37) (SEQ ID NO: 28), and Lys¹⁸ (SEQ ID NO: 29).
- 6. The isolated nucleic acid of Claim 1 wherein the heterologous signal sequence is a sequence selected from the group consisting of: a signal peptide sequence and a leader sequence.
- 7. The isolated nucleic acid of Claim 6 wherein the leader sequence is derived from a protein selected from the group consisting of: a cytokine, growth factor, colony stimulating factor, a clotting factor, (PACAP)/Glucagon superfamily and serum protein.
- 8. The isolated nucleic acid of Claim 6 wherein the heterologous signal sequence is selected from the group consisting of: a secreted human alkaline phosphatase (SEAP) signal peptide sequence, a proexendin-4 leader sequence, a pro-helodermin leader sequence, a pro-glucose dependent insulinotropic polypeptide (GIP) leader sequence, a

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pro-insulin growth factor 1 (IGF1) leader sequence, a preproglucagon leader sequence, an alpha-1 antitrypsin leader sequence and an insulin like growth factor 1.

- 9. The isolated nucleic acid of Claim 1 wherein the heterologous signal sequence comprises a furin cleavage site.
- 10. The isolated nucleic acid of Claim 9 wherein the furin cleavage site encodes a peptide selected from the group consisting of: Arg-X-Lys-Arg (SEQ ID NO: 34), Arg-X-Arg-Arg (SEQ ID NO: 35), Lys/Arg-Arg-X-Lys/Arg-Arg (SEQ ID NO: 36) and Arg-X-X-Arg (SEQ ID NO: 37).
- 11. The isolated nucleic acid of Claim 1 wherein the heterologous signal sequence comprises a prohormone convertase (PC) cleavage site.
- 12. The isolated nucleic acid of Claim 1, wherein the nucleic acid is selected from the group consisting of

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a) SEQ ID NO:1;
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- b) SEQ ID NO:3;
- c) SEQ ID NO:5;
- d) SEQ ID NO:7;
- e) SEQ ID NO:9;
- f) SEQ ID NO:11;
- g) SEQ ID NO:13;
- h) SEQ ID NO:15;
- i) SEQ ID NO: 17; and
- j) SEQ ID NO:19.
- 13. The isolated nucleic acid of Claim 1, wherein the precursor GLP-1 has an amino acid sequence selected from the group consisting of:

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	a) SEQ ID NO:2;
	b) SEQ ID NO:4;
	c) SEQ ID NO: 6;
	d) SEQ ID NO:8;
	e) SEQ ID NO:10;
	f) SEQ ID NO:12;
	g) SEQ ID NO:14;
	h) SEQ ID NO:16;
	i) SEQ ID NO: 18; and
	j) SEQ ID NO: 20.
14.	An isolated polypeptide encoded by a nucleic acid of Claim 12.
15. GLP-1	An isolated precursor glucagon-like peptide 1 (GLP-1) comprising mammalian linked to a heterologous signal sequence.
16.	An isolated precursor glucagon-like peptide I (GLP-1) of Claim 15, wherein the sor GLP-1 has an amino acid sequence selected from the group consisting of:
	a) SEQ ID NO:2;
	b) SEQ ID NO:4;
	c) SEQ ID NO:6;
	d) SEQ ID NO:8;
	e) SEQ ID NO:10;
	f) SEQ ID NO:12;
	g) SEQ ID NO:14;
	h) SEO ID NO:16:

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- i) SEQ ID NO:18; and
- j) SEQ ID NO: 20.
- 17. An expression vector comprising a nucleic acid of Claim 1.
- 18. An isolated host cell comprising a nucleic acid of Claim 1.
- 19. A method of promoting insulin production in an individual in need thereof, comprising administering to the individual an effective amount of a nucleic acid encoding a precursor glucagon-like peptide 1 (GLP-1) comprising mammalian GLP- I linked to a heterologous signal sequence, wherein the precursor GLP-1 is cleaved *in vivo* or *ex vivo* which results in generation of activated GLP-1 in the individual.
- 20. The method of Claim 19 wherein the individual has a blood sugar defect selected from the group consisting of: Type I diabetes and Type II diabetes.
- 21. The method of Claim 20 wherein the nucleic acid encoding the precursor GLP-1 is administered in a viral vector.
- 22. The method of Claim 20 wherein the nucleic acid encoding the precursor GLP-1 is administered as naked DNA.